IN THE UNITED STATES DISTRICT OURT
FOR THE SOUTHERN DISTRICT OF WEST VIRGINIA
CHARLESTON DIVISION

IN RE ETHICON, INC. PELVIC MESH REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION _____ THIS DOCUMENT RELATES TO: ETHICON WAVE 4 CASES LISTED IN DEFENDANTS' EXHIBIT A	Master File No. 2:12-MD-02327 MDL No. 2327 JOSEPH R. GOODWIN U.S. DISTRICT JUDGE

PLAINTIFFS' RESPONSE TO DEFENDANT ETHICON'S MOTION TO EXCLUDE THE OPINIONS AND TESTIMONY OF VLADIMIR IAKOVLEV, M.D.

Plaintiffs in the above-captioned cases respectfully submit this Memorandum of Law in Opposition to Defendant, Ethicon's Motion to Exclude the Opinions and Testimony of Vladimir Iakovlev, M.D. and Memorandum in support thereof ("Def. Br.").

Dr. Iakovlev did not issue a new general report for Wave 4. His opinions are the same as those rendered—and ruled upon by this Court—in Wave 1. The only thing that has changed is those opinions are further supported by Dr. Iakovlev's review of hundreds of additional explanted mesh specimens. As this Court is well aware, the instant motion is just the latest in a long string of attempts by Defendant, Ethicon, Inc. ("Defendant" or "Ethicon") to exclude the opinions of Dr. Iakovlev. Although presented with a few new twists and a hollow claim of "new case law, testing, and scientific literature" (Def.'s Br. at 1), this motion presents the same arguments that this Court has rejected on numerous prior occasions. Scientists, surgeons, engineers and pathologists (including those employed by Ethicon in these same fields) have said the same thing as Dr. Iakovlev for 40 years – polypropylene fibers, including those used in Ethicon's surgical meshes, cracks and degrades after implantation in the human body. No matter how much money Ethicon continues to spend on more and more paid consultants and more and more testing, they can never escape this basic truth. This Court has admonished

Ethicon in the past for repeating already rejected arguments in *Daubert* motions – "Ethicon simply rehashes old arguments and, yet again, essentially asks that I reconsider an earlier decision." Despite this admonishment, Ethicon once again comes to this Court asking it "to rethink what the Court ha[s] already thought through – rightly or wrongly." *Huskey v. Ethicon, Inc*., No. 2:12-cv-05201, 2014 WL 3362287, at *11 (S.D. W. Va. July 8, 2014)(citing *In re C.R. Bard, Inc.*, 948 F. Supp. 2d 589, 649 (S.D. W. Va. 2013). This Court should deny Ethicon's attempt to revive these previously rejected challenges to Dr. Iakovlev's opinions.

The only substantive addition to this Wave 4 brief that was not included in Ethicon's prior briefing is a short section in the beginning—based upon the Fourth Circuit's holding in *Nease v. Ford Motor Co*., 848 F.3d 219 (4th Cir. Feb. 1, 2017)—arguing that Dr. Iakovlev's opinions on the presence of degradation "bark" on explanted meshes should be excluded. Def.'s Brf. at 3-4.[1] But as discussed below, *Nease* did not change the law of this Circuit; it is factually and legally inapposite; and it requires no reconsideration of this Court's prior rulings.

Finally, in this Wave 4 response, Plaintiffs provide additional argument (*infra* at 5-7) in response to Ethicon's assertion that "Dr. Iakovlev's analysis is unreliable because he failed to use a control" (Def.'s Br. at 10-11) based upon Dr. Iakovlev's declaration relating to this issue. Exhibit Ex. T (4/27/17 Declaration of Dr. Vladimir Iakovlev).

I. DR. IAKOVLEV'S OPINIONS IN THIS CASE

Dr. Iakovlev's opinions have not changed for Wave 4. As this Court has previously noted, Dr. Iakovlev is a highly qualified clinical pathologist whose practice involves the examination of 5,000 cases annually. Ex. A, Iakovlev Report at 1. Dr. Iakovlev has reviewed transvaginal mesh samples in connection with his work as a pathologist as St. Michael's Hospital. Ex. A at 2. In addition, Dr. Iakovlev has reviewed mesh samples provided to him in litigation. The testimony and opinions that Dr. Iakovlev offers in this case are substantially

[1] Ethicon also includes a few citations to *Nease* elsewhere in its brief. Def.'s Br. at 1, 5, 6, 9.

the same as those he has previously presented in Court in five separate pelvic mesh trials.[2] Ex. B, Iakovlev 9/11/15 Dep. (Mullins) at 299:15-21. Each of these opinions is well supported with citations to the medical and scientific literature and each is supported by Dr. Iakovlev's own experience as a clinical pathologist reviewing the explanted meshes. He utilized the same "methodology that [he] has previously used when [he] testified in the…southern district of West Virginia…and in other courts where [he] has been allowed to testify at trial." Ex. B. at 298:14-299:4. This methodology has been an acceptable part of clinical pathological practice since the 1920s—and Ethicon itself utilized similar methodology when performing degradation studies of explanted polypropylene as far back as 1983.

II. LEGAL STANDARD

Plaintiffs incorporate by reference the standard of review for *Daubert* motions articulated by the Court in *Edwards v. Ethicon, Inc.*, No. 2:12-CV-09972, 2014 WL 3361923, at **1-3 (S.D.W. Va. July 8, 2014).

III. RESPONSE TO [THE ONLY] NEW WAVE 4 ARGUMENT

A. The Fourth Circuit's Opinion in *Nease* does not change the Court's analysis

Really, the only substantive addition to Ethicon's Wave 1 arguments contained in this Wave 4 brief against Dr. Iakovlev is the inclusion of a discussion of the recent Fourth Circuit opinion in *Nease v. Ford Motor Co.*, 848 F.3d 219, 231 (4th Cir. 2017). However, *Nease* does not change this Court's *Daubert* analysis in any meaningful way. Indeed, the very passages from *Nease* relied upon by Ethicon in relation to *Daubert* standards, including the court's discussion of "testing," are for the most part direct quotes taken from prior—sometimes

[2] *Deborah Barba v. Boston Scientific Corp.*, State of Delaware, Superior Court, C.A. No. N11C-08-050 MMJ (May 19, 2015); *Dianne Bellew v. Ethicon, Inc.*, The United States District Court, Southern District of West Virginia, MDL NO. 2327; 2:12-cv-22473 Charleston, WV, USA (March 5, 2015); *Amal Eghnayem et al. v. Boston Scientific Corp.*, The United States District Court, Southern District of West Virginia, MDL NO. 2326; 2:13-cv-07965 Miami, Florida, USA (Nov. 6, 2014); *Maria Cardenas v. Boston Scientific Corp.*, Commonwealth of Massachusetts, Superior Court MICV2012-02912, Boston, Massachusetts, USA (August 18, 2014); and, *Jennifer Ramirez v. Ethicon Inc.*, State of Texas, Dist. Ct., 2012-CI-18690, Bexar County (April 19, 2016)(by *de bene esse*).

decades-old—Fourth Circuit opinions. *See e.g.*, Def's Brf. at 4 (*citing Nease* quoting *Oglesby v. Gen. Motors Corp.*, 290 F.3d 244, 249 (4th Cir. 1999)).

Ethicon fails to provide any discussion of how *Nease* serves to change this Court's prior analysis of, or rulings on, Dr. Iakovlev's opinions. After spending several paragraphs discussing the facts and holding in *Nease*, Ethicon simply states: "[i]n applying the teachings of *Nease* to Dr. Iakovlev 'bark' theory, it is clear that the Court should preclude his opinions as unreliable for the same reasons." Def.'s Brf. at 4.

"Testing," however, has long been a factor considered by courts when considering the reliability of an expert's opinion. But there is no *requirement*, in *Nease* or elsewhere, that an expert must perform testing on a product—it is just one of the factors taken into account. Indeed, as the Fourth Circuit reiterated in *Nease*, an expert may support his or her opinions through "evidence such as test data[3] *or relevant literature in the field*." *Nease*, 848 F.3d at 231 (emphasis added). Dr. Iakovlev has clearly done so. As explained at length below, Dr. Iakovlev's "bark" opinions are reliable—he and other scientists have *seen* the bark on explanted mesh and confirmed its properties through a panoply of well-accepted processes.

This first-hand knowledge and support Dr. Iakovlev has provided for his opinions makes *Nease* easily distinguishable. In *Nease*,[4] the court premised its ruling on numerous deficiencies in plaintiff's expert's opinions and testimony that simply do not exist in this case. For example, plaintiff's expert in *Nease* primarily relied upon a Ford FMEA that did not even apply to the model year of the car (2001 Ford Ranger) at issue. *Nease*, 848 F.3d at 224-25, 226, 232. Moreover, he acknowledged that: (1) during his examination of the plaintiff's car, he did

[3] In *Nease*, the court merely focused on plaintiff's expert's lack of testing of the purported defect because there was no other support provided. *Id.* at 231 ("Testing was of critical importance *in this case*….) (emphasis added).
[4] *Nease* is also legally distinguishable because, in that case, the plaintiff argued that *Daubert* did not even apply to the expert's testimony—and the Fourth Circuit took issue with the district court's ruling for not properly considering the expert's testimony under *Daubert*. *Nease*, 848 F.3d at 230. That has never been an issue with this Court's rulings in this TVM litigation.

not observe the conditions he opined could result in the malfunction; (2) the part at issue in plaintiff's car operated correctly during his examination of it; and (3) he had never—in plaintiffs' car or any other car—observed the defective condition he claimed could exist. *Id.* at 225-226, 231-32. In fact, plaintiff's expert could not even distinguish a working part from a non-working part in videos shown to him during trial. *Id*. at 226. In *Nease*, unlike here, the plaintiff's expert's theories were completely hypothetical and without support.

In its Order on Ethicon's Wave 1 challenge to Dr. Iakovlev's "bark" opinions, the Court "reserve[d] ruling until Dr. Iakovlev's methodology of examining mesh explant samples can be evaluated firsthand at trial." Dkt. No. 2710 at 7.[5] Nothing has changed that would warrant a departure from that reservation of ruling. No new deposition testimony has been cited. No new opinions have been disclosed. And, as explained above, there has been no change in the law. As such, there is no justification for excluding Iakovlev's testimony on the record that currently exists.

IV. PLAINTIFFS' WAVE 4 RESPONSE TO "CONTROL SLIDE" ARGUMENT

The Court should reject Defendants' argument that Dr. Iakovlev's opinions are unreliable because he has not analyzed a control slide, in addition to analyzing the pathology slides that accompany each Plaintiff's explanted mesh. Plaintiffs recognize that the Court previously held as follows, with regard to Ethicon Wave 1: "To the extent that Dr. Iakovlev offers complications opinions based on his examination of explanted mesh samples without the use of a control sample, his complications opinions are **EXCLUDED**." *In re: Ethicon Inc. Pelvic Repair Sys. Prod. Liab. Litig.*, No. 2327, 2016 WL 4582228, at *4 (S.D. W. Va. Sept. 1,

[5] It is notable that Ethicon has previously filed, and lost, substantially similar previous *Daubert* challenges to Dr. Iakovlev's opinions concerning the presence of degradation "bark" on explanted meshes. For instance, in *Edwards*, Ethicon "argue[d] that Dr. Iakovlev did not sufficiently test Ms. Edwards's mesh to determine if the 'bark' he saw was degraded polypropylene." The Court, in rejecting the argument, found that: "Dr. Iakovlev is a pathologist, not a materials scientist. He makes his determinations by processing and analyzing explants from the human body. As additionally discussed above, the process Dr. Iakovlev used to analyze the explant is the industry standard in pathology." *Edwards*, 2014 U.S. Dist. Lexis 92316 at 69-70.

2016). But Plaintiffs respectfully submit that this ruling should be reconsidered.

Previously, the Court rejected the argument that healthy tissue from the same sample would constitute a "control." *Id.* But the bigger issue—which may not have been effectively raised in the past—is that there is no need for a control sample at all, for a pathologist's opinions to be reliable. As stated in Dr. Iakovlev's attached declaration, the use of a control sample is not appropriate for a **diagnostic** pathology work. As Dr. Iakovlev states, "[d]oing so would make our work impossible as a practical matter." Ex. T at ¶ 5.

Pathology is not a science isolated from medicine. Pathologists are medical doctors who receive additional training in laboratory science. *Id.* at ¶ 6. As stated in a leading textbook, pathology focuses on four areas: (1) the cause of the disease process; (2) the mechanisms of development; (3) the biomechanical and structural alterations induced in the cells and organs of the body; and (4) the clinical manifestations of these changes. *Id.* at ¶ 7. Pathologists' work goes most directly to the third aspect of that sequence, identifying the morphological changes. (*Id.* at ¶ 8). In doing that analysis, pathologists "use their knowledge of normal anatomy and histology (not controls) to detect the changes (abnormalities) and classify them as either the cause (etiology) or the result (disease)." *Id.* In other words, pathologists like Dr. Iakovlev do not need a control sample to look at nerves, tissue, or blood vessels under a microscope and determine whether those nerves, tissue, or blood vessels are damaged. *Id.* at ¶¶ 9-10.

Thus, when Dr. Iakovlev examines a subject, he searches for deviations from normal histology, such as scarring and inflammation. Then, those changes are assessed to determine whether they can explain the patient's symptoms. *Id.* at ¶ 1. For instance, in evaluating the cause of a urinary obstruction, scar tissue around the mesh would indicate sling tightening, and would reveal the mesh as the cause of the obstruction. However, a finding of a tumor would negate a finding of the mesh as the cause. *Id.*

As to controls, pathologists do not regularly have access to control samples, so their "control" is their knowledge of normal presentation, which is then compared to their analysis of specimen. *Id.* at ¶12. To use one example submitted by Dr. Iakovlev, there could never be a control body for an autopsy. Similarly, there are rarely normal samples available to compare to surgical specimens and biopsies. *Id.* One can clearly see how this would be the case with regard to mesh specimens. A true "control" would be a sample explanted from a woman who has experienced no discomfort or other complications. But it would make no sense to explant the mesh from a woman experiencing no complications.[6]

Dr. Iakovlev relies on his knowledge of histological features that have been recognized as abnormal in the scientific literature. *Id.* at ¶ 19. For instance, scarring and foreign body reaction have been described in the literature since the 1800s. *Id.* He also analyzes nerves as they appear in the tissue. *Id.* Dr. Iakovlev uses the same procedures in each case, whether his work is for litigation or purely for treatment purposes. *Id.* at ¶21. His declaration further states that "as a trained physician, pathologist and scientist, I am well aware of the different types of controls and I use them appropriately." *Id.* at ¶20.

The fundamental focus of the *Daubert* inquiry is whether the expert has employed the same "intellectual rigor" in his work for the case as he would in normal practice. *See Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 152 (1999). That is precisely what Dr. Iakovlev has done for these cases. He has reviewed the pathology slides and compared what he is seeing to a normal presentation, exactly as he would do in treating a patient at St. Michael's Hospital. He then takes that information and relates it to the patient's symptoms, as described above.

[6] Dr. Iakovlev's declaration also explains how the use of controls varies depending on the purpose of the pathology being performed. For instance, technical controls are sometimes used to ensure the quality of the staining. *Id.* at ¶13. Subject control groups may be used for research purposes. *Id.* at ¶14. Even with regard to research, asymptomatic patients do not always make for successful controls, because they may have a condition but not exhibit symptoms. *Id.* at ¶¶16-17. For diagnostic purposes, as in these cases, pathologists rely on their knowledge of normal histology to detect abnormalities; to determine the clinical effects of pathological changes; and to exclude alternative pathological conditions. *Id.* at ¶18.

V. RESPONSE TO ETHICON'S [REASSERTED] WAVE 1 ARGUMENTS

As stated above, a comparison of Ethicon's Wave 1 and Wave 4 briefs reveals that the only substantive addition to Ethicon's Wave 1 arguments contained in its recent Wave 4 challenge to Dr. Iakovlev's opinions is a short section on the Fourth Circuit's holding in *Nease*, and a few additional citations to *Nease* throughout the remainder of the brief. As such, Plaintiffs' arguments below substantively mirror those contained in their Wave 1 briefing.[7]

A. Dr. Iakovlev's degradation opinions are based on his training, research, published literature, and experience, as well as the published medical literature, and are therefore reliable.

Dr. Iakovlev offers opinions in his general expert report that Ethicon's transvaginal meshes, like other transvaginally-implanted polypropylene meshes, have the potential to degrade in a woman's body after implantation. Ex. A at 8-11.[8] In support of that opinion, Dr. Iakovlev cites to dozens of published scientific articles and numerous Ethicon documents in his 30-page reliance list to support his opinions. Far from reaching conclusory or unsupported opinions, Dr. Iakovlev painstakingly details his degradation opinions, supporting each such opinion with a wealth of published literature as well as internal Ethicon degradation testing and Ethicon sworn testimony. Dr. Iakovlev also prepared slides and photomicrographs of explants to demonstrate that the degradation of polypropylene reported in the literature can and does occur when Ethicon's mesh is implanted into women for the treatment of pelvic organ prolapse and stress urinary incontinence. Ex. A at 19. ¶¶ 19-27. For each of these opinions, Dr. Iakovlev: (1) reviewed explanted mesh from Wave One Plaintiffs; (2) prepared and reviewed that pathology using the same professional standards and protocols used by him as a clinical pathologist at St. Michael's Hospital; (3) provided detailed photomicrographs of the explanted

[7] Plaintiffs have removed some language to fit within the page limits for this brief.

[8] Dr. Iakovlev's *Mullins* consolidated report contains virtually the same expert opinions as those in his Wave 1 (and therefore Wave 4) general report and as those in his previous general pathology expert reports. His *Mullins* deposition taken on 9/11/2015 related to his general pathology opinions regarding Ethicon transvaginal meshes, and thus, is applicable to his subject Wave 4 general opinions.

meshes as representative images of the degradation and changes that can occur *in vivo*; (4) supported his opinions with specific reference to the medical and scientific literature; and (5) provided Ethicon with the ability to review the pathology slides that he had created from the explanted meshes. Defendant's present attempt to attack and exclude Dr. Iakovlev's opinions is not supported by the facts of this case, the realities of the work that Dr. Iakovlev has done, nor the law controlling *Daubert* challenges.

In an effort to eliminate all degradation opinions, Ethicon again incorrectly asserts that "[a]ll other pathology opinions Dr. Iakovlev seeks to offer about the existence of degradation depend on this purported observation [of bark]." Def. Br. at 4. That same "mischaracterization" was rejected as "misleading" in the Court's Wave 1 Order. Dkt. No. 2710 at 6. In reality, Dr. Iakovlev's opinion that Ethicon's mesh products degrade *in vivo* are based on the well-documented medical and scientific literature that he cites in his report, as well as the Ethicon documents that confirm the existence of degradation. And this Court has previously determined these degradation opinions to be admissible.[9]

B. Dr. Iakovlev's opinions concerning degradation "bark" are reliable

Ethicon's challenge to Dr. Iakovlev's degradation "bark" opinions are without merit. The Court reserved ruling on this issue in Wave 1 so that it could evaluate the evidence "firsthand at trial." Dkt. No. 2710 at 7. No new evidence has been submitted for the Court to consider, but Ethicon continues to suggest that Dr. Iakovlev's opinions regarding the propensity of Ethicon's mesh to degrade in the human body (as indicated by histological staining of the samples) are speculative because he has not completed additional laboratory (*in vitro*) testing by "intentionally oxidizing pristine [out of the box] Prolene…." Def. Br. at 5.

[9] *See Eghnayem v. Boston Sci. Corp*., 57 F. Supp. 3d 658, 671-672 (S.D. W. Va. 2014) (finding that a clinical pathologist like Dr. Iakovlev has "sufficient knowledge to provide expert testimony about the chemistry and surgical pathology of materials like transvaginal mesh. . . . [and] by examining the mesh explants under a microscope, [a clinical pathologist] has witnessed the polypropylene's chemical changes. . . . He is qualified to testify about mesh degradation, mesh shrinkage, and mesh migration.")

Dr. Iakovlev need not do any further confirmatory laboratory testing to support what he and other scientists see in the actual mesh explanted from human beings in order to withstand a *Daubert* challenge. However, Ethicon seeks to use the fact that Dr. Iakovlev continues to study degradation in explanted meshes as part of his medical and academic practice as a basis to challenge his opinions—claiming his ongoing research somehow undermines the reliability of his current opinions. *Daubert* simply does not warrant such a counter-intuitive challenge. Scientific principles are not discredited by the fact that scientists continue to do research in their field. Moreover, Dr. Iakovlev's continued study is intended to determine whether he can replicate *in vitro* what he sees *in vivo* and will study the *in vitro* degradation using the same methodology and tests that he uses to study the *in vivo* degradation. Ex. B. at 45:17-46:13. This testing is not designed to examine any "hypothesis" related to the opinions offered in this case or to prove any degradation opinions—as additional bases are not necessary.

Defendant blatantly misrepresents Dr. Iakovlev's deposition testimony regarding this laboratory experiment and his interest in and reason for doing it. Def. Br. at 2 ("admitted…he failed to test that hypothesis), and 5 ("admitted that he had not conducted this testing"). In actuality, Dr. Iakovlev testified that the testing was unnecessary to support his opinions. Ex. C, *Stubblefield* Dep. Tr. 64:19-65:15. ("That experiment was not required to detect degradation layer for any of these cases. It's done for completely different purpose." … "…it's not needed. I'll do it for different purpose. That experiment is mainly to show that the model of *in vitro* degradation which can simulate *in vivo* degradation is usable. It's more of a testing of the model rather than confirming the degradation."). Contrary to Ethicon's arguments, Dr. Iakovlev never admitted that he failed to conduct some test that would prove or disprove one of his "theories."[10]

[10] Dr. Iakovlev also answered numerous questions during his Mullins deposition about testing of intentionally oxidized polypropylene that had not been implanted or exposed to formalin. He explained that he was not basing any of his opinions on any part of that experiment. Ex. B, at 39:16-23. Dr. Iakovlev actually testified that he is conducting this ongoing experiment with approximately 20 pieces of mesh for which he used a protocol published

Because Dr. Iakovlev has applied the same principles and methodology in these Wave 4 cases as he has in all of his previous cases, this Court should deny Defendant's motion.

C. Ethicon's experts' disagreement with Dr. Iakovlev's opinions do not render them inadmissible

Ethicon's argument that its own paid experts have "disproven" Dr. Iakovlev's opinions is without merit. Ethicon may be permitted to argue its own experts' theories to the jury; but at this stage, what the Court is presented with are, at best, conflicting opinions of experts. Such disagreements do not warrant exclusion of an expert under *Daubert*. *Edwards v. Ethicon,* 2014 U.S. Dist. Lexis 92316, 69-70 (S.D. W. Va. 2014) ("[M]ere disagreement among experts is not, in itself, a reason to exclude an expert's testimony.").

Furthermore, Ethicon's claims that its experts have conducted *in vitro* testing that disproves Dr. Iakovlev's *in vivo* opinions are false. Ethicon has already admitted in this litigation, through its expert Robyn Prueitt, Ph.D., that *in vitro* tests cannot replicate the *in vivo* environment. Ex. D, Prueitt Deposition at 89:21-90:2 ("in vitro it's naked cells in a petri dish being exposed directly to this chemical, whereas in the body the mesh is on cells, but there, you know, is a circulatory system, ***there's many other things going on in vivo that the in vitro tests cannot replicate."***). Despite its own expert's statements, Ethicon asserts the Court must exclude Dr. Iakovlev's opinions because *its* latest *in vitro* test results did not replicate what Dr. Iakovlev has observed *in vivo.* These conflicting opinions are, at best, incorrect.

Undeterred by the concessions made by Dr. Prueitt, Ethicon simply hired more

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in a journal. *Id.* at 31:20-33:15. His purpose was to test the published protocol by submerging the mesh pieces into solutions of hydrogen peroxide with catalysts and in solutions of acids in a dark room cabinet in order to see if these solutions would degrade the outside of the mesh fibers. *Id.* at 32:1-33:12; 44:12-20. Based on Dr. Iakovlev's research and his experience in analyzing hundreds of explanted polypropylene meshes, he has decided to keep the samples in the solutions for 18 months because the cracked outer layer of polypropylene or "bark" becomes most visible after 12 months. *Id.* at 33:16-34:4; 41:2-9. When asked more specific questions about certain aspects of the experiment, he testified that he would not be able to recall all of the specifics without checking the paper, the protocol and the jars themselves. *Id.* at 34:8-14; 34:21-35:1; 35:23-36:4. But importantly, just as he had testified in the *Stubblefield* case, Dr. Iakovlev reiterated that this lab experiment was not part of his opinions and not necessary to confirm or expound upon his opinions as stated in his Report.

"experts" to do more testing, which they again assert disproves Dr. Iakovlev's opinions. Exponent[11] material scientist, Dr. Steven MacLean, presents Ethicon's most recent degradation "test" results.[12] Ethicon's arguments here are inapposite because Dr. MacLean did not even do the test that Dr. Iakovlev is currently undertaking, despite Ethicon's representation to the contrary. Dr. MacLean only incubated and oxidated samples *for up to 5 weeks*. Ex. F, MacLean Report at 15. However, Dr. Iakovlev testified at his deposition that in order for H&E staining and polarized light to show degradation bark on a pristine mesh sample that had been oxidized *in vitro*, such samples had to be incubated for "*at least a year and a half* because I believe that that's how much time you need to make it visible by my techniques." Ex. B at 41:5-8 (emphasis added); *see also* Ex. B. at 42:4-44:1 (confirming that H&E staining and polarized light can only be used to detect degradation bark after samples have been incubated for at least eighteen months). Ethicon cannot credibly argue that the five-week test conducted by Dr. MacLean shows anything—let alone that Dr. Iakovlev is wrong.

D. Dr. Iakovlev's methodology is well supported by the medical and scientific literature

The methodology used by Dr. Iakovlev to review the specimens for degradation has been recognized as the industry standard by this Court and has been utilized by Ethicon for nearly 40 years. Ethicon's claim that there is no scientific or medical evidence to support Dr. Iakovlev's opinions concerning degradation "bark" from explanted mesh *in vivo* is simply wrong. No matter the specific terminology that has been used by other scientists, dozens of peer-reviewed articles have demonstrated that polypropylene degrades in the body.[13] In other words, Dr. Iakovlev is not alone in his scientific research or his opinions in this case regarding

[11] Exponent, has been paid nearly **$4,000,000.00** to do "testing" for mesh defendants in these MDLs. (Reitman Trial Tr. 47:5-48:5, *Sherrer v. Truman Med. Center Inc.* Cir. Ct of MO, Jackson Co. Case no. 1216-cv-27879).
[12] Plaintiffs' filed a Motion and Memorandum to Exclude the Opinions and Testimony of Defendant Ethicon, Inc.'s Expert Steven MacLean, PhD., P.E. [Docket # 139]. To the extent the Court considers Dr. MacLean's opinions relevant to its *Daubert* analysis for Dr. Iakovlev, Plaintiffs incorporate those arguments by reference herein.
[13] "Bark" is simply a descriptive term Dr. Iakovlev uses to describe the cracked outer layer of polypropylene fibers.

the fact that polypropylene, including Ethicon's polypropylene, degrades in tissue.[14]

Under a *Daubert* analysis, the dispositive question here is not, as Ethicon posits, whether Dr. Iakovlev's **conclusions** of degradation "bark" have been previously published in the medical and scientific literature. Instead, the appropriate question is whether Dr. Iakovlev utilized established, reliable **methodology** when studying the explanted mesh samples and when arriving at his opinions.[15]

This Court has previously found that the methodology Dr. Iakovlev used to detect degradation "bark" is reliable: "the process Dr. Iakovlev used to analyze the explant is the industry standard in pathology." *Edwards*, 2014 U.S. Dist. Lexis 92316, at 70. Specifically, the methodology used by Dr. Iakovlev to review the specimens for degradation – H&E staining and polarized light – has been individually peer reviewed. Moreover, these same methodologies have also been utilized by Ethicon's own scientists to look for degradation in Prolene. Ex. A. at 8-9; Ex. B at 302:8-20, 303:9-18. In fact, Smith et. al. reported and depicted polarized micrography identifying birefringent (refractile) mesh as the foreign body inciting tissue reaction in a series of explanted vaginal meshes at the University of Michigan.[16]

Ethicon's own internal documents attest to the reliability of the methodology, findings, and opinions of Dr. Iakovlev. Interestingly, despite its knowledge of these studies, Ethicon fails to reference any of them in its moving papers. (*See, e.g.*, 1983 study conducted by Ethicon demonstrating that Prolene degrades using the same histological preparations, light microscopy and polarized light as used by Dr. Iakovlev.).[17] In the studies conducted by

[14] *See* Ex. G, Reliance List attached to Dr. Iakovlev's report. *See also*, Ex. H, page 5 from Exhibit 21 of Dr. Iakovlev's 04/19/16 *de bene esse* (containing a list of doctors and scientists that have published in peer-reviewed literature that polypropylene degrades in human tissue.)

[15] *Eghnayem v. Boston Sci. Corp.*, 57 F. Supp. 3d 658, 669 (S.D. W. Va. 2014).

[16] Smith, T. et al. Pathologic evaluation of explanted vaginal mesh: interdisciplinary experience from a referral center. Female Pelvic Med Reconstr Surg 19, 238-41 (2013). (Ex. A. at 11).

[17] ETH.MESH.15955438 (attached as Ex. I). *See also* Ex. A. at 9 ("The findings lead Ethicon's scientists to conclude that Prolene degrades forming an outer layer of degraded material and the cracking observed on the surface of Prolene by scanning electron microscopy is altered polypropylene and not proteinatious material.")

Ethicon, arrows are directed toward the cracked surface of the fiber in exactly the same fashion as the images that Dr. Iakovlev has described in his peer- reviewed publications and in all his reports, including his Wave One Report.[18] The Ethicon scientist who authored the study stated that she would be "happy to show these at the next **PROLENE Microcrack Committee Meeting**." (emphasis added)

In 1984, the "Ethicon Research Foundation" conducted yet another internal study regarding the cracked outer layer of explanted Ethicon Prolene (polypropylene) sutures.[19] This study also did histological staining of formalin-fixed explanted polypropylene and used light microscopy and polarized light microscopy to analyze and study the cracked, degraded fiber. These Ethicon scientists used a histopathological stain known as "Phloxine" to stain the samples for pathological microscopic analysis and found "severe" cracking in the suture material that had been implanted for the longest time period. Ex. K at 2-3. Again, Ethicon scientists published microphotographs that look almost identical to those that Dr. Iakovlev has published in both his expert report and in his peer-reviewed publications.[20]

Ethicon's polypropylene is dyed blue during the manufacturing process so that the surgeons can better see the fibers during surgery. Dr. Iakovlev opinion that the cracked outer layer of the fibers, or "bark," is degraded polypropylene (Ex A at 18 with images at 84-94)—and not human protein material, as is argued by Ethicon's experts—is, astonishingly, the same conclusions reached by these Ethicon scientists over 30 years ago: "The cracked layer appeared blue in gross specimens and **blue dye particles** were evident in histological sections of the layer. **This would indicate that the layer is dyed PROLENE polymer and not an isolated protein coating on the strands."** Ex. K at 4; *see also* Ex. A at 9-10. These Ethicon studies, done long before the present transvaginal mesh litigation began, utilize the same

[18] ETH.MESH.15955439 (attached as Ex. J)
[19] ETH.MESH.15955462 (attached as Ex. K)
[20] Ex. H; Ex. A at 84-86 and 91.

methodology as Dr. Iakovlev, and reached substantially the same findings. Ethicon criticism of Dr. Iakovlev's use of the very same microscopic and light polarization techniques—utilized by its own scientists—is absurd. And Ethicon's use of this methodology undermines the opinions and test results of its highly-paid litigation "experts" at Exponent and, in fact, can be fairly interpreted to *disprove* their creative and unsubstantiated hypotheses.[21] [22] Because the methods and techniques utilized by Dr. Iakovlev are not new or novel; are widely accepted in the medical community; and, are well accepted in the peer-reviewed literature (and evidently, well accepted by Ethicon's own scientists well before the litigation began), his methodology is sound and his conclusions are admissible.

Ethicon, through its paid Exponent consultant, Dr. MacLean, takes issue with the staining methods used by Dr. Iakovlev by claiming that certain features "can" be produced by manipulation of the microscope; "can" cause the "appearance of lines" around the fibers; and "can" lead to differences in fiber thickness in samples. Def. Br. at 7. But these are merely opinions of one scientist; there is no "methodology" employed.[23]

If Ethicon wants to bring forth its latest theory that Dr. Iakovlev, his colleagues and, presumably, Ethicon's own scientists, through conspiracy or manipulation, improperly used the

[21] Ethicon conducted other internal degradation studies over the years. It conducted a 10-year dog study that began in 1985. Ex. L at 10. During that study, Ethicon's scientists concluded "the PROLENE surface, intact at the two year point, showed signs of degradation at five years." Inconsistent with the opinions of Ethicon's experts, its *employee* scientists determined—as did Dr. Iakovlev—that the sample preparation was not what caused the cracking: "it can be said unequivocally that the cracking that was seen in any of the sutures was not introduced by sample preparation, *i.e.*, drying. If cracking was observed on a dry suture in the light microscope or in the SEM, the same cracking was also found on the same suture after it had been in body fluids and then in sterile water, without ever having dried." *Id.* Moreover, formaldehyde (formalin) was not used in the dog study—further undermining Ethicon's experts' claims that the cracking observed on the explanted Ethicon mesh devices is caused by a formaldehyde/protein bond at the surface of the fiber. *See also*, Ex. A at 10.

[22] Ethicon's pathologist in its preclinical department for 30 years, Dr. Thomas Barbolt, provided sworn testimony that the antioxidants used by Ethicon to protect its Prolene fibers from degradation in the body can leach out of the fibers into the host (human) tissue. Barbolt Depo. Tr. 360:20-361:6 (01/08/14) (Ex. O). He also testified that it was known that Prolene could undergo surface degradation before 1992. *Id.* at 409:10-13.

[23] When combined with the Phloxine staining done by Ethicon's scientists in its own "bark" testing over 30 years ago, this totals *six* different pathological staining methods, all utilized by pathologists in their daily practices and all of which come to the same conclusion: histological staining of various types all show that polypropylene fibers degrade in the body. Ramirez Iakovlev Trial Tr. 387:2-388:12 (Ex. P).

microscope and made up all of these findings, cross-examination at trial would be the proper forum to further such theories; but not in a *Daubert* motion. Conversely, in his peer-reviewed article, *Degradation of Polypropylene In Vivo*, Def. Br. at Ex. F, Dr. Iakovlev uses *five* different types of standard histological staining, all of which show cracking in the outer layer of the fiber.

E. Dr. Iakovlev's opinion that degradation causes clinical complications is well supported and reliable

Ethicon next argues that even if its mesh does degrade, Dr. Iakovlev cannot correlate that degradation to any clinical complications. In doing so, Ethicon misrepresents the record, the scientific literature, and Dr. Iakovlev's own training and expertise.

Dr. Iakovlev is qualified, by virtue of his training and experience as a clinical pathologist, to opine on the correlation between clinical complications and pathology review. Indeed, that is his everyday job. As this Court has previously noted in connection with a previous Ethicon *Daubert* challenge to Dr. Iakovlev:

> A pathologist is a clinician who provides diagnoses for patient care based on the examination of specimens they receive and relevant clinical information. Dr. Iakovlev testified that "[e]verything which is taken out of the human body or taken off a human body at the time of death comes for a pathology co-examination, so we have to correlate the devices with the changes in the body, and this is part of our training as pathologists." According to Ethicon's expert Dr. Zheng vaginal mesh "just represent[s] a kind of foreign body" for a pathologist to examine. "[A] pathologist typically deals with many kinds of foreign or medical device[s] removed or explanted from patients . . . . So overall TVT or mesh-related product is part of those medical devices removed and then submit [ted] to the pathology department. The[] pathologist has expertise to examine them[.]" [Ethicon's Expert Dep. at 46.] Dr. Zheng has also testified that pathologists can help diagnose clinical problems, including symptoms such as pain and bleeding.

Edwards, 2014 U.S. Dist. Lexis 92316, at 68-69. Dr. Iakovlev's job requires him to "provide clinical consultations to physicians at St. Michael's Hospital, which requires [him] to examine pathology specimens, review clinical information relating to the patient, and reach conclusions about the cause of a patient's injuries or illnesses… [He is] also knowledgeable in the areas of chemistry, hematology, microbiology, serology, immunology and other special laboratory

studies as they relate to my practice of pathology." Ex. A at 1. Thus, by virtue of his education, training, and experience as a clinical pathologist, Dr. Iakovlev is qualified to testify about the correlation between explanted mesh pathology and clinical complications, potential injuries, and pain in patients.

Finally, Ethicon's out of context citations to Dr. Iakovlev's acknowledgment of contrary positions do not support a conclusion that his opinions are unreliable. Instead, they show that Dr. Iakovlev has taken into account the "contrary scientific literature" and has not "selectively [chosen] his support from the scientific landscape", a requirement under *Daubert. Wilkerson v. Boston Sci. Corp.*, 2015 U.S. Dist. LEXIS 58671, 24-25 (S.D. W. Va. May 5, 2015). Furthermore, *Daubert* does not require an expert's opinions to be irrefutable; and this Court has recognized that an expert can reach an opinion based on the weight of evidence despite contrary reports in the medical literature—precisely what Dr. Iakovlev has done.

F. Dr. Iakovlev's opinions concerning complications are reliable

Ethicon also takes issue with Dr. Iakovlev's opinions concerning the correlation between Ethicon's meshes and complications in general. A clinical pathologist can reliably draw a correlation between a finding from a pathologic exam and the clinical symptomology of the patients. *Edwards*, 2014 U.S. Dist. Lexis 92316, at 68-69. Ethicon's challenge to those opinions must be rejected for several reasons: (1) Ethicon misrepresents the methodology used by Dr. Iakovlev; (2) the "methodology" suggested by Ethicon is not consistent with methodology utilized in the medical and scientific community; (3) Dr. Iakovlev's opinions are consistent and supported by the medical and scientific literature.

Dr. Iakovlev's opinions are that Ethicon's mesh can cause complications in women—not that it always does. As Dr. Iakovlev described, "[t]he purpose of the report was to analyze the device as a whole, not the individual patients." Ex. B. at 222:8-10. In his report and deposition, Dr. Iakovlev testified about what phenomena were visualized upon pathologic

review from Ethicon mesh explants (*e.g.*, roping and curling, Ex. B at 216:15-25; scar encapsulation and scar filling, Ex. B. at 223:11-12). Dr. Iakovlev's opinions are that the observations on the slides are "abnormal" and that the abnormality is a "mechanism for symptoms" and that such symptoms "can happen." Ex. B. at 225:1-3. This is precisely the type of information that is relevant to the causation and design defect claims before the jury.

Additionally, Dr. Iakovlev did not "fail to account for" relevant scientific literature. His report relies on over 600 scientific articles and Ethicon documents – including literature that he himself has authored. Ignoring those reliance materials, Ethicon claims that Dr. Iakovlev's opinions must be stricken because it has found a single article it believes to be relevant that was not included on his extensive reliance list. *See* Def. Br. at 11-13. Failure to include a single article in expert report's reliance list does not serve as the basis to strike opinions. *Tyree v. Boston Scientific Corp.*, No. 2:12-cv-08633 at 74-75 (S.D. W. Va. October 29, 2014).

G. Dr. Iakovlev's opinions concerning pain complications and mesh folding/deformation are reliable

Ethicon has previously challenged Dr. Iakovlev's pain and deformation opinions, and that challenge has been rejected by this Court. *Edwards*, 2014 U.S. Dist. Lexis 92316, at 69-70. Despite that ruling, Ethicon now urges this Court to simply adopt their neuropathology "experts'" disagreement with Dr. Iakovlev concerning pain mechanisms as the basis for a *Daubert* challenge. However, differing conclusions reached by opposing experts is not an appropriate challenge under *Daubert* and Ethicon's motion should be denied.[24]

Similarly, Ethicon misrepresents the record when it asserts that Dr. Iakovlev cannot

[24] Ethicon's arguments regarding pain border on the absurd. Def. Br. 16-18. In essence, it argues that some nerves cause pain, but just not these pelvic nerves. It is irrefutable that bodies sense pain from nerves; that transvaginal mesh causes pain in a significant number of women; and that surgeons who remove mesh due to focal pelvic pain remove mesh that often contains the very nerves that were causing the pain. Further, in a woman's pelvic tissues (vaginal mucosa), there exist both sensory and motor nerve strands that are entwined or "mixed" together like electric lines with positive, negative and ground wires all entwined together and thus, a distinction between these types of nerves is irrelevant to Dr. Iakovlev's opinions. *See* Ex. P, *Ramirez* Tr. Tr. 30:24-32:16; 40:1-19; 64:9-67:21; 70:1-73:06; *see also* Ex. A. 11-12 and 15-16.

support his opinion that mesh deforms. Def. Br. at 18. This opinion not "novel" as Ethicon asserts. Dr. Iakovlev cites to eight (8) separate articles supporting his deformation opinions, including one peer-reviewed article that Dr. Iakovlev himself co-authored. Ex. A at 12. Furthermore, he has provided actual proof—in the form of pathology slides from explanted mesh—that Ethicon's mesh becomes encapsulated in scar tissue and deforms. Ex. A at 22-25. The fact that Ethicon's experts have conflicting opinions is of no import to this motion.

H. Dr. Iakovlev's opinions concerning erosions leading to infection are reliable

It is scientifically undisputed that when transvaginal mesh migrates and irritates the vaginal mucosa (layer of tissue lining the vagina), it breaks down the mucosa thereby causing an "erosion" (i.e., the mesh "erodes" through the tissue.). Ex. A p. 17-18. Erosions are one of the most common mesh-related injuries and are a complication unique to mesh surgeries. *Id.* In essence, the erosion and extrusion of the mesh through the vaginal mucosa becomes an open wound in the vagina that contains hundreds of different types of bacteria.[25]

Ethicon has long known of the association of erosions to infections—both from its pathology consultant of over 15 years, Dr. Bernd Klosterhalfen, as well as from its surgical group in France (the so-called "French TVM Group") who co-invented the Prolift System with Ethicon.[26] But now, in context of litigation, Ethicon refuses to acknowledge this decades-old knowledge, choosing instead to simply have their hired "experts" criticize Dr. Iakovlev and point to irrelevant CDC findings as their "support" for a request to exclude his opinions in this regard. Again, Defendant's experts disagreement with Dr. Iakovlev (and its own pathologist and key opinion leaders/co-inventors) is not cause for exclusion of his opinions.

I. Dr. Iakovlev's mesh samples are relevant and reliable

Finally, Ethicon asserts Dr. Iakovlev seeks to opine about mesh he "cannot identify."

[25] Hankins dep Ex. Q 3/9/15 88:15-90:17.
[26] ETH.MESH. 00006636; ETH.MESH.02157879 (attached as Ex. R); Berrocal, J., et al. *Conceptual advances in the surgical management of genital prolapse.* J Gynecol Obset Biol reprod 2004: 33:577-587 at page 5 (Ex. S).

Def. Br. at 20. In reality, as spelled out clearly in the Expert Report itself:

> For the opinions and figures in this report, I have relied on my findings in the explant specimens, including those transvaginal devices manufactured by Ethicon. In addition, I have also relied on data available in peer reviewed publications, including my own peer reviewed publications.

Ex. A at 5. This was confirmed at Dr. Iakovlev's deposition:

> **Q.** Now every one of the photomicrographs that appear in Exhibits 1 and 2 to today's deposition, that is your report and supplemental report, did every one of those photomicrographs appear either from prior expert reports in Ethicon litigation, in the specific pathology of the consolidated plaintiffs, or in peer-reviewed medical literature written by you?
> **A. That's correct. These are the three sources.**
> **Q.** And you've been asked questions today about identifying various -- what you called additional TVT cases in your report; do you recall those questions?
> **A. Yes, I do.**
> **Q.** Did you produce photomicrographs of the additional TVT cases in the course of other reports you've provided in TVT cases?
> **A. Yes, I did.**

Ex. B at 297:20-298:13. Furthermore, Ethicon's claim that the report is partially based on "mesh not at issue in this litigation" (Def. Br. at 20) is patently false. Dr. Iakovlev testified clearly that the opinions that he was being questioned on at his deposition were based on TVT-R and TVT-O devices, both made by Ethicon and both made with the same material – Prolene. As he explained at his deposition, it did not make a difference if the product was a TVT-R or a TVT-O because the mesh itself is "exactly the same" and that "in terms of pathological findings . . . there is [no] reason for making a distinction between the two devices." Ex. B. at 297:23-298:12.

CONCLUSION

For the reasons stated herein, Plaintiffs respectfully request that the Court DENY the defendants' Motion to Exclude the Testimony of Dr. Iakovlev in its entirety.

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Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on April 27, 20176, I electronically filed the foregoing document with the Clerk of the court using CM/ECF system which will send notification of such filing to the CM/ECF participants registered to receive service in this MDL.

/s/ Edward A. Wallace